Remarks

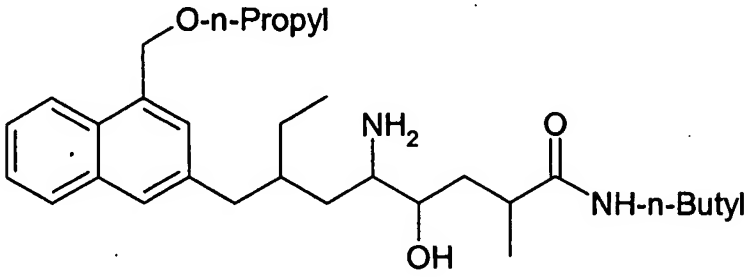
Further and favorable reconsideration is respectfully requested in view of the foregoing amendment and following remarks.

Thus, claim 6 has been cancelled, rendering the objection to this claim in item 2 on page 3 of the Office Action moot.

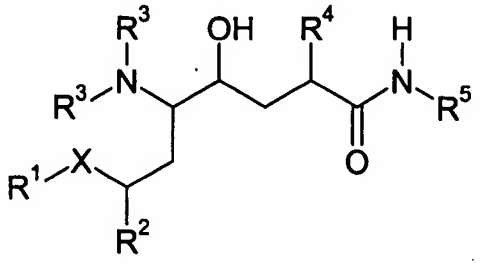
The patentability of the presently claimed invention over the disclosure of the reference relied upon by the Examiner in rejecting the claims will be apparent upon consideration of the following remarks.

Thus, the rejection of claims 1-7 under 35 U.S.C. §102(b) as being anticipated by Goeschke et al. (CAPLUS Abstract Accession Number 1995:995373/ EP 678503) is respectfully traversed.

The EP '503 reference, which is cited on page 1 of the present application, teaches the following compound:



This compound does correspond to a compound of instant formula (I) of the present application,



(I)

wherein X = CH_2, R^1 according to group (B) is a "polycyclic, unsaturated hydrocarbon radical" (napthalene) which is substituted by methylpropoxy, R^2 = ethyl, R^3 = H, R^4 = methyl, and R^5 = n-butyl.

However, instant Claim 1 includes the following proviso at the end of group (B):

"where, in the case that R^1 is naphthyl or cyclohexenophenyl, at least the ring of said R^1 radicals not bonded directly to X is substituted as specified"

The reference compound having the structure set forth above does not bear a substituent at the ring not bonded to X (CH_2). That is, the substituent (methylpropoxy) on the naphthyl group is on the ring bonded to X, but there is no substituent on the ring not bonded to X.

Thus, the proviso in claim 1 excludes the reference compound, as a result of which the reference fails to anticipate this claim, as well as claims 2-7 dependent thereon.

The rejection of claims 1-7 under the first paragraph of 35 U.S.C. §112 is respectfully traversed.

The Examiner states in item 6 that the instant invention "involves pharmaceutical compounds for inhibiting enzymes". Further "inhibiting enzymes is a very unpredictable art" as "very slight perturbations in the structure of an inhibitor... can have radical effects on the binding of an inhibitor".

Also according to the Examiner "applicant provides no working examples".

The Examiner requests Applicants to clarify for the record which experiments and tests were actually performed and to indicate the particular compounds used, and he concludes that "the claims are clearly not enabled for the full scope of the compounds claimed", and recommends either amending the claim scope or providing additional data to "guide one of ordinary skill in the art to compounds possessing the asserted utility".

In response to the lack of enablement rejection, please see the enclosed TEST REPORT providing evidence that the instantly claimed compounds are in particular effective as renin inhibitors.

The specification also describes the claimed compounds as renin inhibitors which show inhibitory effects in *in vitro* systems with minimal concentrations of about 10^{-6} to about 10^{-10} mol/l (page 16, lines 9-10).

The test report provides proof that the instantly disclosed compounds show inhibitory effects in *in vitro* systems with minimal concentrations of about 10^{-6} to about 10^{-10} mol/l. The data provided shows that these compounds are indeed very effective. For example, the instant Example 3DD has an IC_{50} value of 5.5 nM = 5.5 x 10^{-9} mol/l (see 12th example on page 2 of the enclosed test report). The "3" in Example 3DD refers to Example 3 for the 40 residues for R^1 as

shown in the table in the description beginning on page 20. The "DD" in Example 3DD refers to Example DD for the residues for NHR^5 as shown in the table in the description beginning on page 30. The resulting formula for Example 3DD is shown on page 45.

For these reasons, Applicants take the position that the rejection of the claims under 35 U.S.C. §112 should be withdrawn.

The Examiner has provisionally rejected claims 1-7 for obviousness-type double patenting as being unpatentable over claims 12-20 and 22-23 of Serial No. 11/992,132. The Examiner is kindly requested to hold this rejection in abeyance, pending an indication that the claims of the present application are otherwise in condition for allowance.

Therefore, in view of the foregoing amendment and remarks, it is submitted that each of the grounds of objection and rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

Respectfully submitted,

Peter HEROLD et al.

By 

Michael R. Davis
Registration No. 25,134
Attorney for Applicants

MRD/pth
Washington, D.C. 20005-1503
Telephone (202) 721-8200
Facsimile (202) 721-8250
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TEST REPORT

General description

Inhibition of renin in plasma (hPI) are determined by the *in vitro* assay as described in the instant English description on page 15ff. The test used is the one according to Nussberger et. al (1987) *J. Cardiovascular Pharmacol.*, Vol. 9, p. 39-44. The compounds of the present invention show inhibitory effects in in vitro systems with minimal concentrations of about 10^{-6} to about 10^{-10} mol/l.

Example #	hPI IC_{50} (nM)
1K	2.2
3K	3.5
34K	2.6
5K	1.9
3H	23.6
1H	35.0
12K	12.8
2G	19.5
2K	5.9
8K	3.9
13K	10.6
13H	336.0
34B	49.5
5B	30.6
3A	5.4
3B	6.3
3C	4.0
3F	2.1
3G	2.2
5A	12.1
5D	11.5
5G	21.7
5H	13.4
3D	4.1
34A	31.7
34C	32.0
34D	29.5
34G	71.1
34F	24.8
34H	14.8
4A	36.9
4B	30.2
4D	31.0
4G	19.9

Example #	hPI IC_{50} (nM)
4C	20.7
4H	22.0
4k	5.4
7G	7.6
7A	4.1
7B	3.9
7H	10.5
7K	1.5
9A	3.2
9B	3.2
9H	2.7
3DD	5.5
9VV	6.5
9TT	2.9
7VV	5.9
3VV	6.6
7TT	7.0
3TT	5.8
3VV	1.4
7VV	1.4
3Y	14.4
6H	245.0
9VV	1.6
6VV	30.4
17H	13.7
17VV	3.8
29H	242.0
30H	303.0
29VV	12.2
30VV	30.8
5VV	4.8
40H	1.3
40VV	0.8
22H	23.8
40XX	0.6
32VV	5.8
22VV	8.8
23VV	0.7
32XX	4.0
36VV	0.6
36XX	2.1
37XX	1.1
37H	3.7
37K	1.1
37VV	1.2
40K	0.7